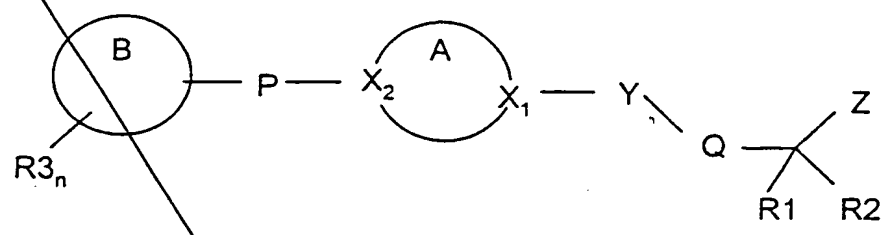
CLAIMS:

What we claim is:-

1. A compound of the formula I




I

wherein ring B is a monocyclic or bicyclic alkyl, aryl, aralkyl, heteroaryl or heteroaralkyl ring comprising up to 12 ring atoms and containing one or more heteroatoms independently chosen from N, O, and S; alternatively ring B may be biphenyl; ring B may optionally be linked to ring A by a C1-4 alkyl or a C1-4 alkoxy chain linking the 2-position of ring B with a carbon atom alpha to X2;

each R3 is independently selected from hydrogen, halogen, NO2, COOR wherein R is hydrogen or C1-6alkyl, CN, CF3, C1-6 alkyl, -S-C1-6 alkyl, -SO-C1-6 alkyl, -SO2-C1-6 alkyl ,C1-6 alkoxy and up to C10 aryloxy, n is 1,2 or 3;

P is -$(CH_2)$n- wherein n = 0, 1, 2, or P is an alkene or alkyne chain of up to six carbon atoms; where X2 is C, P may be -Het-, -(CH[R6])n-Het-, -Het-(CH[R6]n-or -Het-(CH[R6])n-Het-, wherein Het is selected from - CO-, -S-, SO-, -SO2-, -NR6- , or -O- wherein n is 1 or 2, or P may be selected from -CO-N(R6)-, -N(R6)-CO-, -SO2-N(R6)- and -N(R6)-SO2-, and R6 is hydrogen, C1-6 alkyl, up to C10 aralkyl or up to C9 heteroalkyl;

Ring A is a 5-7 membered aliphatic ring and may optionally be mono- or di-substituted by optionally substituted C1-6 alkyl or C1-6 alkoxy, each substituent being independently selected from halogen, C1-6 alkyl or an oxo group;

X1 and X2 are independently selected from N and C, where a ring substituent on ring A is an oxo group this is preferably adjacent a ring nitrogen atom;

Y is selected from -SO2- and -CO-;

Z is -CONHOH , Y is -CO- and Q is selected from -C(R6)(R7)-, -C(R6)(R7)-CH2-, -N(R6)-, and -N(R6)-CH2- wherein R6 is as defined above, and solely in relation to Q as here defined, R6 may also represent up to C10 aryl and up to C9 heteroaryl, and R7 is H, C1-6

alkyl, or together with R6 forms a carbocyclic or heterocyclic spiro 5, 6 or 7 membered ring, the latter containing at least one heteroatom selected from N, O, and S;

Z is -CONHOH, Y is -SO2- and Q is selected from -C(R6)(R7)-, and —C(R6)(R7)-CH2-;

or Z is -N(OH)CHO and Q is selected from -CH(R6)-,-CH(R6)-CH2-, and -N(R6)-CH2-;

R1 is H, or C1-6 alkyl;

Z is selected from -COOH, -CONHOH, -N(OH)CHO and N(OH)COR wherein R is C1-6alkyl, up to C10 aryl and up to C9 aralkyl

and R2 is a heterocyclylalkyl ring having 5-7 ring atoms and comprising one or two ring heteroatoms independently selected from oxygen, nitrogen and sulphur, the ring being optionally substituted by (i) Y-R9 wherein R9 is C1-6 alkyl, up to C10 aryl, up to C12 aralkyl or up to C12 heteroaryl(hetero)alkyl, or (ii) Y-T-R9 wherein Y and R9 are as previously defined and T is oxygen or N-R8 wherein R8 is hydrogen or C1-6 alkyl, the heteroatom(s) being independently selected from oxygen, nitrogen and sulphur; R9 and R8 independently being optionally substituted by one or two groups selected from halogen, NO2, CN, CF3, C1-6 alkyl, -S-C1-6 alkyl, -SO-C1-6 alkyl, -SO2-C1-6 alkyl and C1-6 alkoxy;

or a pharmaceutically-acceptable salt or in vivo hydrolysable precursor thereof.

2. A compound as claimed in claim 1 and wherein:

ring A is a 5-6 membered aliphatic ring and is optionally mono- or di-substituted by optionally substituted C1-6 alkyl or C1-6 alkoxy, each substituent being independently selected from halogen, C1-6 alkyl or an oxo group;

R3 is hydrogen, halogen, NO2, CF3, C1-4 alkyl, and C1-4 alkoxy;

n is 1 or 2;

ring B is monocyclic or bicyclic cycloalkyl, aryl, aralkyl or heteroaryl having up to 10 ring atoms;

P is -(CH2)n- wherein n is 0 or 1, or P is -NH-CO-;

one or both of X2 and X1 = N;

Y is -SO2- or -CO-;

Q is -CH(R6)-, -CH(R6)-CH2-, -N(R6)-, and -N(R6)-CH2- wherein R6 is hydrogen or C1-6 alkyl; when Q = -N(R6)-, or -N(R6)-CH2- then Y may also be -CS-, also Q may be linked to R1 or R2 to form a 5-7 alkyl or heteroalkyl ring;

R1 = hydrogen, or C1-4 alkyl.

Z = -CONHOH- or -N(OH)CHO

and R2 is a heterocyclylalkyl ring having 5-7 ring atoms and comprising one or two ring heteroatoms independently selected from oxygen, nitrogen and sulphur, the ring being optionally substituted by (i) Y-R9 wherein R9 is C1-6 alkyl, up to C10 aryl, up to C12 aralkyl or up to C12 heteroaryl(hetero)alkyl, or (ii) Y-T-R9 wherein Y and R9 are as stated in claim 1 and T is oxygen or N-R8 wherein R8 is hydrogen or C1-6alkyl, the heteroatom(s) being independently selected from oxygen, nitrogen and sulphur; R9 and R8 independently being optionally substituted by one or two groups selected from halogen, NO2, CN, CF3, C1-6 alkyl, -S-C1-6 alkyl, -SO-C1-6 alkyl, -SO2-C1-6 alkyl and C1-6 alkoxy;

or a pharmaceutically-acceptable salt or in vivo hydrolysable precursor thereof.

3. A compound as claimed in claim 1 and wherein:

R3 is hydrogen, chlorine, fluorine, NO2, CF3, methyl, ethyl, methoxy, ethoxy;

ring B is phenyl, biphenyl, napthyl, pyridyl, pyrimidinyl, pyrazinyl and pyridazinyl;

P is a direct bond;

both X2 and X1 are N;

Y is -SO2-;

Q is -CH2-;

R2 is a heterocyclylalkyl ring having 5-7 ring atoms and comprising one or two ring heteroatoms independently selected from oxygen, nitrogen and sulphur, the ring being optionally substituted by (i) Y-R9 wherein Y is as stated in claim 1 and R9 is C1-6 alkyl or alkylamino, up to C10 aryl or arylamino, up to C12 aralkyl or aralkylamino, up to C12 heteroaryl(hetero)alkyl, R9 independently being optionally substituted by one or two groups selected from halogen, NO2, CN, CF3, C1-6 alkyl, -S-C1-6 alkyl, -SO-C1-6 alkyl, -SO2-C1-6 alkyl and C1-6 alkoxy;

R1 is hydrogen;

Z is -N(OH)CHO;

or a pharmaceutically-acceptable salt or in vivo hydrolysable precursor thereof.

4. A compound as claimed in claim 1 and wherein:

R3 is methoxy, fluorine or 4-fluoro;

ring A is unsubsituted;

ring B is phenyl, pyridyl, or 2-pyridyl;

R2 is optionally substituted 3-piperidinyl, 4-piperidinyl or N-substituted 4-piperidinyl, wherein the substituents are as stated in claim 3;

or a pharmaceutically-acceptable salt or in vivo hydrolysable precursor thereof.

Sub B1

5. A compound as claimed in claim 1 and wherein R2 is 3- or 4-piperidinyl, optionally N-substituted by Y-R9 wherein Y is as stated in claim 1 and R9 is C1-4 alkyl or alkylamino, C6 aryl or arylamino, up to C10 aralkyl or aralkylamino or up to C10 heteroaryl(hetero)alkyl, R9 independently being optionally substituted by one or two groups selected from halogen, CF3, and C1-4 alkyl;

or a pharmaceutically-acceptable salt or in vivo hydrolysable precursor thereof.

6. A pharmaceutical composition which comprises a compound of the formula (I) as claimed in claim 1 or a pharmaceutically acceptable salt or an in vivo hydrolysable ester and a pharmaceutically acceptable carrier.

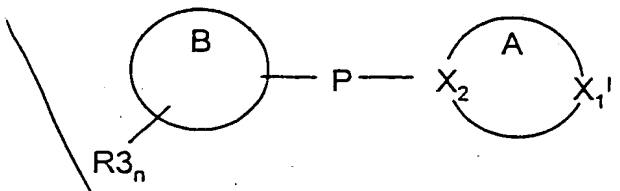
7. A compound of the formula (I) as claimed in claim 1 or a pharmaceutically acceptable salt or in vivo hydrolysable ester thereof for use in a method of therapeutic treatment of the human or animal body.

Sub B1

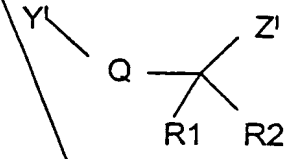
8. A method of treating a metalloproteinase mediated disease condition which comprises administering to a warm-blooded animal a therapeutically effective amount of a compound of the formula (I) or a pharmaceutically acceptable salt or in vivo hydrolysable ester thereof.

9. A process for preparing a compound of the formula (I) or a pharmaceutically acceptable salt or in vivo hydrolysable ester thereof which process comprises

a) reacting a compound of the formula (II) or a pharmaceutically acceptable salt or in vivo hydrolysable ester thereof with a compound of the formula (III)




II




III

wherein $X_1'$ represents X or a precursor of X (whether by modification or displacement) or an activated form of X suitable for reaction with $Y_1$;

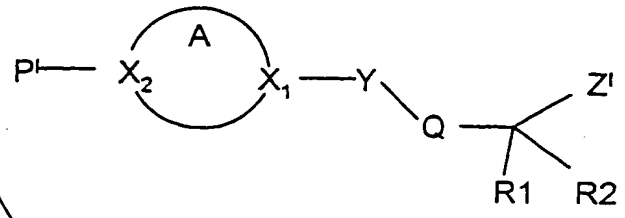
$Y_1$ represents Y, a precursor of Y, or an activated form of Y suitable for reaction with $X_1'$;

by way of non-limiting example, when X is C then $X_1$ may be derivatised to include a precursor of Y for reaction with a compound of formula III wherein $Y'$ is a precursor of Y;

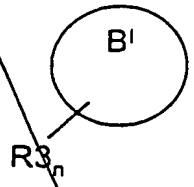
$Z'$ represents a protected form of Z, a precursor of Z (whether by modification or displacement of $Z'$) or an activated form of Z;

or

b) reacting a compound of the formual (IV) ) or a pharmaceutically acceptable salt or in vivo hydrolysable ester thereof with a compound of the formula (V).




IV




V

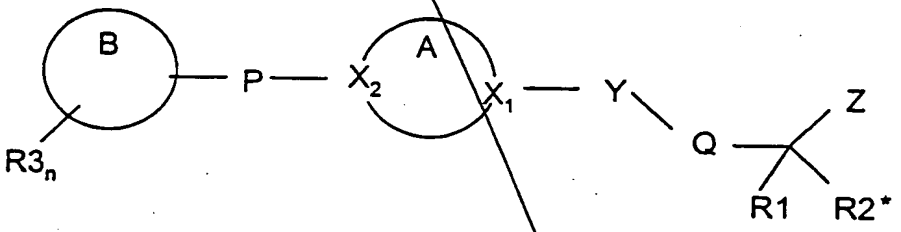
wherein $B^I$ represents a suitable ring function or substituent group for reaction with $P^i$;

$Z^I$ is as hereinbefore defined; and

$P^i$ represents a suitably activated form of the linker P for reaction with $A^I$;

or

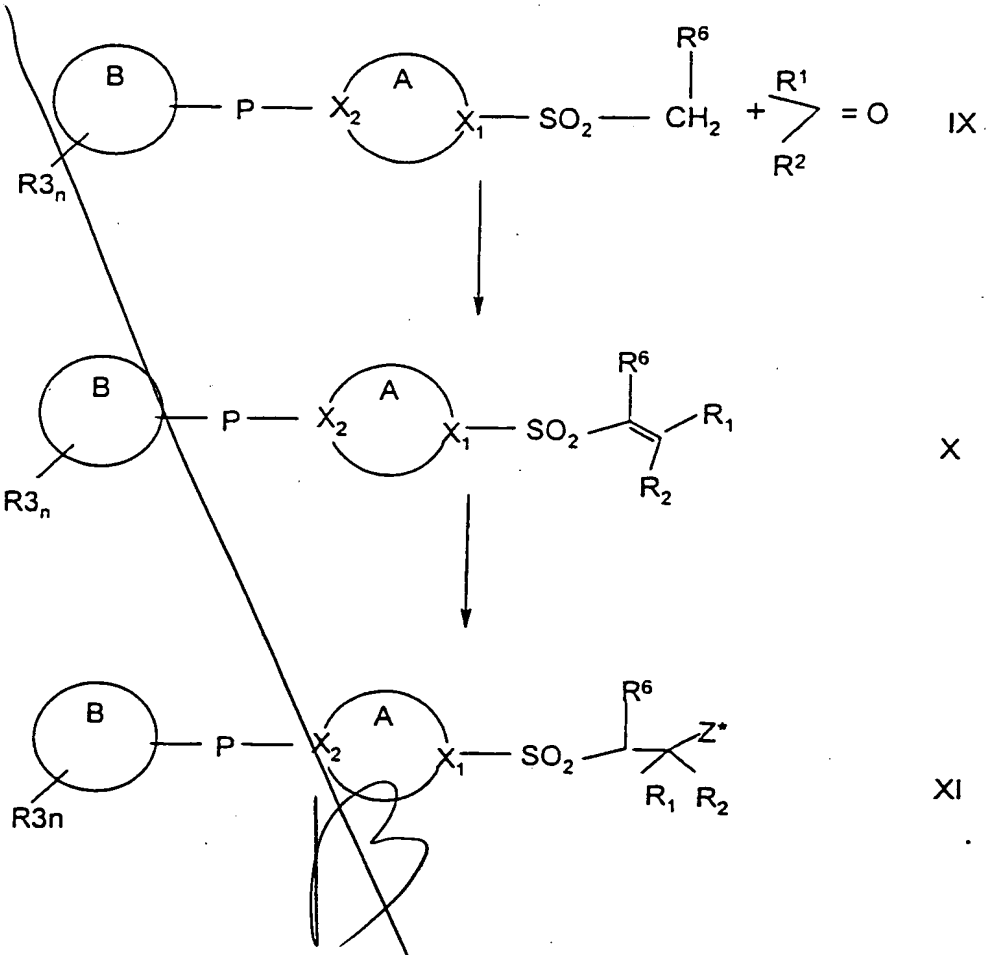
c) reacting a compound of the general formula (VIII)




wherein R2* is a precursor for R2 with appropriate reagent(s) in one or more steps to yield R2. The group Z is conveniently protected during such steps. By way of non-limiting example R2* is a piperidine or piperazine ring;

or

(d) reacting a compound of the formula IX with an appropriate compound of the formula R1-CO-R2 to yield an alkene of the formula X, which is then converted to a compound of the formula XI wherein Z* is a hydroxylamine precursor of the group Z, and then converting Z* to the group Z, all as set out below:




10. The use of a compound of the formula (I) or a pharmaceutically acceptable salt or in vivo hydrolysable precursor thereof in the preparation of a medicament for use in a disease condition mediated by one or more metalloproteinase enzymes.

11. The use of a compound of the formula (I) or a pharmaceutically acceptable salt or in vivo hydrolysable precursor thereof in the preparation of a medicament for use in the treatment of arthritis.

12. The use of a compound of the formula (I) or a pharmaceutically acceptable salt or in vivo hydrolysable precursor thereof in the preparation of a medicament for use in the treatment of atherosclerosis.

add B1